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A CASE OF ACROMEGALY, WITH REMARKS ON THE PATHOLOGY OF THE DISEASE.[1]

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MRS. A. B., aged 42, came to Denver in May, 1893, to consult Dr. John Chase about her failing vision, and was referred to me for neurological examination and treatment.

Her father is in perfect health, aged 70; his parents both survived the eighty-fifth year, and his brothers and sisters show no hereditary taint. Her mother died at fifty-four and her mother's mother at seventy-one, both of consumption. The maternal grandfather and maternal aunts and uncles have been healthy and long-lived.

The patient first menstruated at fifteen. Menstruation was generally profuse and painful; otherwise she was perfectly well until twenty-eight years of age, when her only child was born. This child, who is now quite well, was weaned soon after his birth. Menstruation returned seven months after the weaning, but was then scant and irregular, disappearing finally when the patient was thirty.

Soon after parturition pain and cramping sensations in the right leg and toes became annoying. About the time menstruation ceased a decided lack of endurance was noticed and severe headaches began to occur, the pain being at the vertex or just back of the eyes, mostly steady, but sometimes of a shooting character. At times the patient felt as though the blood was rushing to her head and crowding the eyes out of their sockets. There has been much suffering from headache ever since.

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[1] Read by title before the American Neurological Association, Washington, D. C., May 1894.

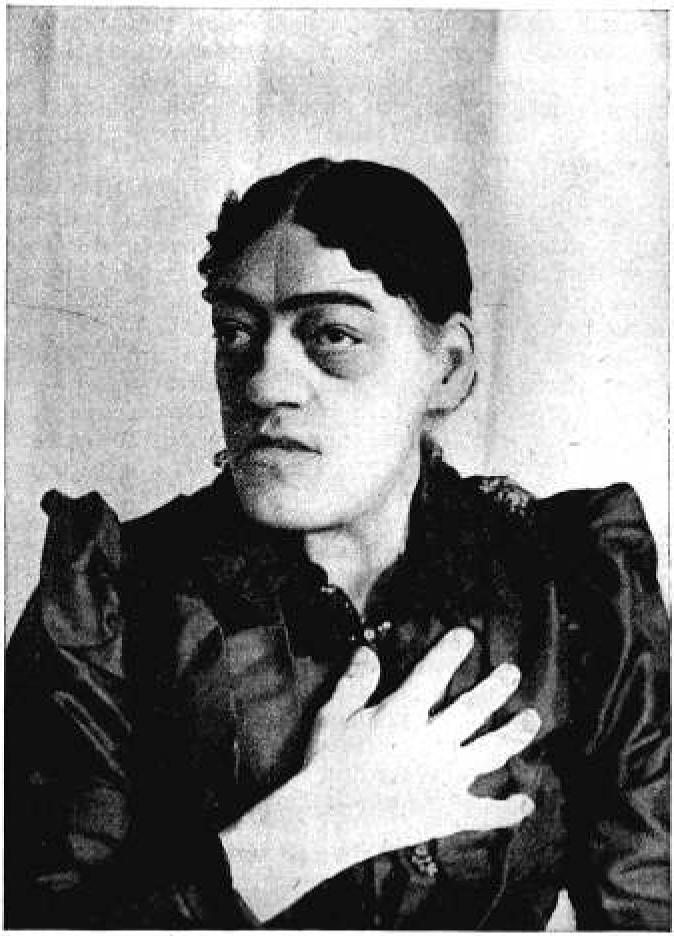
Before this she had been very slender, her waist measure being twenty-one inches, and her weight only ninety-eight pounds. Now, a decided enlargement of the abdomen, with increase of weight, was noticed. At the age of thirty-two she began to have shooting pains in the hands, and the joints of the fingers were enlarged. She could no longer button her clothing. This was supposed to be "rheumatic gout," but it soon became evident that the entire hand was growing larger. The size of gloves increased from No. 6¼ to No. 8½, The feet were increasing in size at the same time, and No 5 shoes were required instead of No. 3, which was formerly the proper size.

When about thirty-two years of age vision began to fail in the right eye, and this eye has since become totally blind. One half of the field was lost before the other. On first telling of this the patient was very positive that the right (temporal) half of the field was the first to disappear, indicating with her hand the blind and the good sides as she recalled how things appeared to that eye. Afterward she was not so sure as to which side first grew dark, but I believe her first account to be correct. The left eye, which now shows distinct temporal hemianopsia, was not noticeably defective until March, 1892. Whether its temporal field disappeared before or after the loss of the nasal field of the right eye can not be ascertained from the history. Soon after the defect in vision was first noticed there began to be a roaring in the ears, synchronous with the pulse, which has persisted, more or less, ever since.

When she was thirty-five years old the gums began to recede from the teeth. Three years later, on account of pain in the jaws, fifteen teeth were extracted. Only two were left, and as the pain continued these were also extracted, but without benefit. It was now apparent that the lower jaw projected beyond the upper one.

For the past five or six years there have been attacks of palpitation of the heart with dyspnœa; of late they have somewhat abated. At times there has been very profuse sweating.

Condition, May, 1893. The patient is five feet five inches in height, and weighs one hundred and forty pounds. Her general appearance is very striking, suggesting acromegaly at the first glance. The face is long and massive. The eye-balls are prominent and the lids large and puffy. The nose is very long and its lower part much enlarged. The lips are thick, with the aperture of the mouth wide, while the lower jaw is much too long for the upper.



The hands, while not much elongated, are decidedly thicker and broader than normal, the fingers having the characteristic "sausage shape." The feet are also broad and thick, but not so large, in proportion, as the hands.

The neck is somewhat bent forward. The larynx is not prominent. The thyreoid gland can barely be felt; it seems smaller than normal. Speech is slow and drawling, with the voice rather high pitched.

The clavicles at their sternal ends are enlarged. The scapulæ show nothing abnormal. The sternum is long and broad; its manubrium appears to be dislocated backward. The pelvis, judging from external measurements, is flattened in its antero-posterior diameter, but is otherwise normal. There is no marked abnormality of the lower limbs except the size of the feet.

The skin and nails are normal. Sweating was formerly very profuse, but is not so now. The hair of the head is abundant, and has grown thicker during the progress of the disease; on the other hand, hair has almost entirely disappeared from the pubes and axillæ. There are no glandular enlargements.

The pulse ranges from seventy to ninety-six; it is regular though small. The first heart sound is soft; otherwise the sounds are normal. Cardiac percussion dullness is normal, and there is no dullness over the sternum. The temperature, taken on two occasions, was 97.8° F. There are periods of excessive thirst. Appetite and digestion are good except for obstinate constipation. Judging by percussion dullness, the liver is small while the spleen is of normal size.

The urine contains no albumen or sugar.

Muscular power is diminished in the lower limbs generally; in the arms it is fair considering the general condition. There is no facial paralysis, and the tongue, which is very large, is protruded in the median line. The plantar reflex is present, and the knee-jerk and Achilles-jerk exaggerated on both sides. There is slight but distinct ankle-clonus on the left side and a trace of clonus on the right.

Sensibility to touch, pain and temperature is retained throughout the body. There is an excessive sensibility to cold, and the patient complains of coldness of the ears. Taste and smell are good. Hearing is nearly normal, though slightly impaired in the right ear. Tinnitus is annoying.

The right eye is totally blind. Vision in the left is so impaired that the patient can no longer read, although she can see enough to avoid objects in moving about the room. The outer side of the visual field is blind, the line of demarcation between it and the inner side being sharply defined.

The pupils are equal, and both react to light falling on the left eye. There is no paralysis of the extra-ocular muscles, but the right eye wanders out from lack of fixation. The left optic disk is in a condition of advanced atrophy; the right disk is still more atrophic, the largest vessels being mere threads. There is lachrymation during the attacks of pain back of the eyes. The lids are puffed but not œdematous.

The mental condition appears somewhat dulled, and the patient is at times rather irritable; but there is no marked defect of memory, and, on the whole, she bears her pain and faces the hopelessness of her miserable situation remarkably well.

MEASUREMENTS.

Skull: Circumference, 58 cm.; binauricular arc, 37.8 cm.; naso occipital arc, 36.5 cm.; naso-bregmatic arc, 14.3 cm.; antero-posterior diameter, 19.5 cm.; transverse diameter, 14.8 cm.; cephalic index, 75.9 cm.; glabella to chin, 14 cm.; glabella to margin of hair, 7 cm.; upper incisors to occipital protuberance, 19.5 cm.; upper incisors to bregma, 20.2 cm.; bregma to occipital protuberance, 16.8 cm.; empirical height of cranium, 15.5 cm.; length of nose, 6 cm.; width of mouth, 6 cm.; alveolar border of lower jaw to tip of chin, 3.6 cm.; temporo-maxillary articulation to tip of chin, 13.6 cm.; angle of jaw to tip of chin, 11 cm.; between angles of jaw, 10.6 cm.;

Limbs, right side: Acromion to olecranon, 29 cm.; olecranon to styloid of ulna, 25.5 cm.; around condyles of humerus, 21 cm.; around wrist, 18 cm.; around metacarpo-phalangeal articulations, 21.2 cm.; end of radius to tip of middle finger, 18 cm.; breadth of hand, 9.6 cm.; circumference of arm, 25 cm.; circumference of forearm, 21.5 cm.; crest of ilium to head of fibula, 56.5 cm.; head of fibula to external malleolus, 36 cm.; circumference of thigh, 42 cm.; circumference of knee, 35.5 cm.; patella, 7 x 7 cm.; circumference of calf, 27 cm.; around malleoli, 22.8 cm.; around heel and instep, 30 cm.; around metatarso phalangeal joints, 23.5 cm.; length of foot, 24 cm.; width of foot, 8.8 cm.; length of great toe, 7 cm.

The left limbs are slightly smaller than the right.

Trunk: Circumference of chest on deep expiration, 79 cm.; circumference of chest on full inspiration, 86.5 cm.; length of sternum, 18 cm.; circumference of neck, 35 cm.; between iliac crests, 29 cm.; between iliac spines, 26.7 cm.; external conjugate of pelvis, 17 cm.

Although the patient was able to come to my office on the day of her arrival in Denver, the necessary effort, following her journey, exhausted her very much and she afterward remained in her room, most of the time in bed, until she returned home at the end of a month. The treatment consisted in the administration of codeine, cannabis and acetanilid, with an occasional injection of morphia, to relieve the severe pain in the head. One evening there was a very rapid failure of what vision remained, so that in a few minutes she was almost totally blind. The ophthalmoscope showed no change in the vessels or nerve-head, and by the next day vision was restored to about what it had been before.

In June, 1893, she returned to her home in a distant town. In September, her husband reported profuse sweating and loss of control of the bladder, but with less pain. At this time, following the example of Putnam,[2] thyreoid extract was ordered, but it was too late to fairly test any remedy. In October, pain was again very severe in the head and lower limbs; she could no longer stand and there was no control over the bladder or rectum. Early in November coma gradually came on and ended in death.

I did not know of this termination until it was far too late to make any arrangement for an autopsy.

That this is a genuine case of acromegaly, there can be no question. The gradual enlargement of the hands, feet, nose, jaw and tongue occurs in no other disease. When the patient entered my office, I had just been looking at the pictures of one of Marie's cases of acromegaly, and, as will be readily understood from her photograph, the diagnosis was made in an instant.

Without attempting a thorough discussion of the pathology of the disease, I will call attention to some interesting features of this case.

As in Marie's cases, there is an absence of any apparent hereditary predisposition to the disease. Its duration can be accurately fixed as fourteen years. But this case is interesting mainly because it adds another to the constantly growing list of those which confirm Marie's original belief, that disease of the pituitary body is the cause of acromegaly.

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[2] Transactions of the Association of American Physicians, 1893.

The headache, the optic nerve atrophy with consequent loss of vision, the tinnitus, the paraplegia, and the loss of control of the sphincters, all taken together, can be explained only as the local effects of a growth in the region of the pituitary. Such a growth pressing first on the inner fibres of the optic tracts would cause blindness of the nasal half of each retina, that is of the temporal half of each visual field. It will be remembered that temporal hemianopsia of the right eye was first noticed, and that at the time of examination there was distinct left temporal hemianopsia with complete blindness of the right eye. The loss of the right nasal field was, of course, due to the additional destruction of the outer fibres of the right tract, and a similar destruction of the left tract was evidently going on while the patient was under observation. Such a growth lying between the internal carotid arteries, and pressing on either of them, would cause the rhythmical tinnitus noted. Bilateral pressure on the motor tracts in the crura accounts for the paraplegia and also for the loss of control over the bladder and rectum.

The local diagnosis, then, is clear enough; it is only in regarding the disease of the pituitary body as the cause of the characteristic trophic changes in the limbs and face, that one may be accused of going beyond the evidence.

Here it should be noted that any antecedent improbability of disease of an organ apparently so insignificant causing such widespread disturbance has been removed by the abundant proof that destruction of the thyreoid gland does cause myxœdema. Not only is the clinical resemblance between these diseases so close that acromegaly has been described as myxœdema, but there is also an obvious pathological relation, which should lead us to expect a similarity of causes.

The resemblance between the pituitary body and the thyreoid gland is also exceedingly close. Measured by their long line of descent, both are most aristocratic organs. The mammalian kidney, for example, is but a new-comer in comparison. The most primitive vertebrates known have the beginnings of the thyreoid and pituitary; and in an animal as low as the lamprey, without limbs or jaws, these glands are well developed.

The pituitary, like the thyreoid, starts as a pouch from the wall of the oral cavity, but, growing dorsal, it has been caught between the ossifying centers at the base of the skull, and so is included within the cranium. Before its relation to acromegaly gave it an unexpected importance in pathology, its glandular tubules, lined with active epithelium and filled with colloid matter like the thyreoid follicles, and its abundant blood-supply led comparative anatomists to the conclusion that it must have some important function.

According to the recent researches of Andriezen,[3] it originally poured its secretion into the current of a water-vascular system, which, beginning at the mouth, irrigated the cerebral ventricles and central spinal canal of the earliest vertebrates. The main function of this system must have been respiratory, but the pituitary gland probably furnished some substance necessary for the proper nutrition of the nerve tissue, which it now furnishes directly through the blood and lymph.

Briefly stated, the evidence for the belief that acromegaly is caused by interference with the function of the pituitary body, is as follows: Of eighteen autopsies in supposed cases of acromegaly, the gland was found to be destroyed or diseased in fifteen,[4] while in a very large proportion of other cases there are localizing symptoms distinctly showing that it is involved. Those who do not accept this theory regard the frequent involvement of the pituitary as simply one of the consequences of the disease. They claim, in the first place, that the gland has been found to be normal in genuine acromegaly.

This claim is supported in three of the autopsies mentioned, and in two of the cases the eminence of the reporters gives especial weight to their evidence. The first is that of one of the Hagner brothers, studied during life by Friedreich and Erb, and after death by Arnold, in which both pituitary and thyreoid were normal. This case commonly passes as one of acromegaly, and Marie, who first described and named the disease, originally regarded it as one. Nevertheless, after learning all the facts of the case, Marie[5] is decidedly of the opinion that it is not one of genuine acromegaly, because the jaw, nose, lips, tongue and xiphoid process were not enlarged, the neck was slender, the kyphosis was lumbo-dorsal, instead of cervico-dorsal, and the enlarged extremities were not of the shape characteristic of acromegaly. The second case is that of the patient Mennig, studied during life by Fraentzel, and after death by Virchow. Here the pituitary was normal, except for a slight enlargement scarcely worth mentioning, and the thyroid was also normal. Marie, however, in his paper in *Brain*, July, 1889, said that this case was probably not one of acromegaly, and he and his followers now class both this and the Hagner case as examples of the disease which he has discovered and called hyperthophic osteo-arthropathy of pulmonary origin.

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[3] *British Medical Journal*, January 13, 1894.

[4] The cases in which the pituitary body was found to be destroyed or diseased are those of Brigidi, Henrot, Thomson, Klebs, Broca, Holsti, Bury, Gonzalez-Capeda, Caton and Paul, Marie and Marinesco, Duchesneau, Gautier, Dana, Squance, and Bonardi. It was normal in the cases of Frauetzel, Friedreich, and Erb, and Jarbo. See Osborne, Ref. *Handbook of the Med. Sciences*, supplement, 1893, also Collins, JOURNAL OF NERVOUS AND MENTAL DISEASE, Dec., 1892, Jan. and Feb., 1893.

[5] *Brain*, July, 1889.

A third case in which pituitary and thyreoid were normal has been reported by Sarbo.[6] Here there was no history, but the patient was both tubercular and syphilitic. The jaw, nose and lips do not appear to have been enlarged; the face was broad, not long. The ears were large, the skull was thickened, and the hands and feet were enormous. A true osteitis was found. As far as can be judged from the only description of this case accessible to me, it was not one of acromegaly; the features are rather those of hypertrophic osteo-arthropathy, of pulmonary origin.

It seems, then, that the pituitary body has not been found normal in any case of undoubted acromegaly that has so far been published.

Still, it is said that destruction of the pituitary body by tumors does not cause acromegaly.

Here it should be noted that extreme care would in any case be necessary to determine whether so small an organ were completely destroyed.

A very minute portion of the thyreoid, if left by operation or disease, will prevent the development of myxœdema, and a proportionate amount of the pituitary might easily escape detection. Dercum's[7] citation of Weir Mitchell's[8] case, in which an aneurism apparently destroyed everything in the region of the pituitary, seems open to this objection. There is nothing in the notes of the autopsy to show that remnants of the pituitary were sought, or that acromegaly was thought of at that time.

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[6] Abstracted by Joseph Collins, JOURNAL OF NERVOUS AND MENTAL DISEASE, January, 1893.

[7] *American Journal of the Medical Sciences*, March, 1893

[8] JOURNAL OF NERVOUS AND MENTAL DISEASE, Jan. 1889.

Moreover, it is not true that tumors of the pituitary body never cause acromegaly. In Henrot's case there was a pituitary tumor of some kind. In Bury's case there was a glioma excavating the sella turcica, and a similar growth was found in Caton's case recently reported. Now, a glioma cannot be regarded as an effect of acromegaly, nor can these cases be readily disposed of as coincidences. Under all the circumstances it seems rational to regard the destruction of the pituitary body as the cause of the trophic symptoms.

It does not follow, however, that destruction of the pituitary must always cause acromegaly. Extirpation of the thyroid causes increased growth of the pituitary,[9] and in several cases of disease of the thyreoid associated with myxœdema cretinism the pituitary has been found enlarged.[10] Conversely, Vassale and Sacchi claim to have shown that the thyroid enlarges after removal of the pituitary.[11] If these kindred glands are so co-related that one may assist the other, additional work on the part of the thyreoid might well be sufficient to prevent acromegaly in one case and not in another. The frequency of thyreoid disease in acromegaly, and the fact that Putnam has obtained marked improvement in such cases from thyreoid extract, give support to this hypothesis.

It appears, at present, that the most hopeful treatment of acromegaly is the administration of pituitary bodies from the lower animals. I am very sorry it was not tried in the case here reported.

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[9] Rogowitsch, Arch. d. Phys., 1888, ii, 433; Beitr. z. Path. Anat., Ziegler, 1888, iv.; Stieda. Dissertation, Koenigsberg, both cited by Putnam, Trans. Assoc. American Physicians, 1893.

[10] Hofmeister, Fortschritte d. Medicin, 1892, cited by Putnam l. c.; Collins, JOURNAL OF NERVOUS AND MENTAL DISEASE, Feb. 1893.

[11] Putnam, l. c.